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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,802	03/19/2004	Norbert Schulke	67268-A/JPW/AJD	8894

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EXAMINER	
KIM, YUNSOO	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,802	SCHULKE ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-141* is/are pending in the application.

4a) Of the above claim(s) *42-99 and 111-132* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41,100-110 and 133-141* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Yunsoo Kim, Art Unit 1644, Technology 1600.

2. Claims 1-141 are pending.

3. Upon reconsideration, supplemental species election to further elect one specific amino acid set forth in the office action mailed on 10/23/06 has been withdrawn.

Accordingly, claims 42-99 and 111-132 are withdrawn from further consideration by the examiner 37CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1-41, 100-110 and 133-141 drawn to a pharmaceutical formulation comprising a CD-4 IgG2 chimeric heterotetramer and histidine buffer read on elected species of an amino acid stabilizing agent are under consideration in the instant application.

4. Applicant's claim for domestic priority under 35. U.S.C. 119(e) is acknowledged.

5. Applicant's IDS filed on 12/28/05 has been acknowledged.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out this invention.

7. Claims 1-41, 100-110 and 133-141 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure does not enable one skilled in the art to practice the invention without any undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed.Cir.1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of the skilled in the art to practice the claimed invention.

The intended use of the claimed pharmaceutical formulation is to inhibit infection of CD4 cells by HIV, preventing HIV infections as well as treating HIV infections as described in the specification of the instant application on p. 5-6. As acknowledged by the instant specification p. 2, various mechanisms are involved in infection, such as attachments, dissociating gp 120 from the viral surface or inhibiting intercellular transmission of virus initiated by virus-mediated cell fusion. Thus, prevention of HIV infection cannot be achieved by preventing of entry of HIV virus into human cells.

Letvin (Annu Rev Med.,2005 Feb 56:213-223) teaches that HIV differs from other viruses in terms of controlling cellular or humoral responses because of their rapid replications and containment of HIV replications in infected indiviruals related with HIV specific CTL responses. Because of rapid replication, inhibition of infection of CD4 cells is not successful. In addition, in absence of temporal correlation between early viral control and the failure of development of neutralizing antibody at a high titer, treatment of HIV infection is elusive (p. 215-216, in particular)

Furthermore, Letvin teaches that the development of HIV vaccine which reads on prevention of HIV infection remains challenging as well. Due to the enormous genetic variation of the virus and unusual importance of cytotoxic T lymphocytes, it is still difficult to develop HIV vaccine (abstract, in particular).

In addition, the specification of instant application has not provided any in vitro or vivo data to show the claimed invention in regards to inhibiting infection of CD4 cells by HIV, prevention or treatment of HIV infections.

Therefore, there is insufficient direction as to how to use a pharmaceutical formulation comprising CD4-IgG2 chimeric heterotetramer in histidine buffer in inhibiting infection of CD4 cells by HIV, prevention and treatment of of HIV-1 infection as to whether such a desired effect can be achieved or predicted, as encompassed by the claims.

In view of the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-41, 100-110 and 133-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/04801 (IDS reference) in view of U.S. Pat. No., 5,817,767 (IDS reference).

The '801 publication teaches a stable formulation comprising antibody to various antigens including CD4 (p. 7, lines 10-14, in particular) in 5-20 mM histidine buffer at pH 6 (p. 9, lines 15-17, in particular). The '801 publication further teaches that the antibody concentration being 25-100mg/ml (including 25mg/ml, and 100mg/ml), reconstituted concentration of 150mg/ml (p. 3, lines 4-9, tables 5-6, in particular).

In addition, the '801 publication teaches the formulation being isotonic such as having osmolality of 280mOsm/kg (p.9, lines 6-8, in particular), stable at 2-8°C for at least 2 years, stable at ambient temperature for 6 months and –70°C for 2 years (p. 8-9, p. 30, in particular). The '801 publication further teaches various routes of administration including parenteral such as subcutaneous administsration (p. 17, lines 25-35, in particular), article of manufacture or kit comprising a vial, sealable bottle, syringe (p. 18, lines 17-30, in particular) including diluent, instruction. The '801 publication further teaches monomeric protein percentage is at least 99% (p. 20, table 2, in particular).

Claim 14 is included in this rejection because the referenced formulation is stable at -70°C for more than 2 years and it will be inherently stable at -90°C.

The '801 publication further teaches that above formulation is stable at least 2 years at 2-8°C (p. 8-9, in particular), is suitable for various types of antibodies including humanized, antibody fragments or monoclonal (p. 7-9, in particular) and antibodies to various molecular targets (p. 10-11 overlapping paragraph, in particular) and adds stability and prevents degradation of antibodies (p. 2, in particular).

Furthermore, the '801 publication teaches the antibody solution further comprising glycine at about 25-250 mM, a lyoprotectant such as sucrose at 30mM-250mM, trehalose at 250mM, non-ionic surfactant such as polysorbate at 0.01% (p. 20, Table, in particular) in various combinations.

The claimed invention differs from the reference teachings only by using CD4-IgG2 chimeric heterotetramers.

However, the '767 patent teaches CD4-IgG2 chimeric heterotetramers composition (claims 1-6, in particular).

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to stabilize an CD4-IgG2 chimeric heterotetramers as taught by the '767 patent with a formulation comprising a histidine buffer and stabilizing agent and/or lyoprotectant as taught by the '801 publication.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the '801 publication teaches that a formulation comprising a histidine buffer, stabilizing agent such as glycine and/or lyoprotectant adds stability to any antibodies and prevents degradation of antibodies (p. 7-9, 20, in particular).

From the teachings of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. No claims are allowable.

11. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yunsoo Kim
Patent Examiner
Technology Center 1600
February 9, 2007

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